DOCKET NUMBER 1414.025
PATENT

#48
D.J
6/22/96

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of)
KING et al.)
Serial No. 07/110,791) Group Art Unit: 1807
Filed: October 21, 1987) Examiner: Marschel, A.
For: HUMAN GENE RELATED TO BUT DISTINCT FROM EGF RECEPTOR GENE)

DECLARATION OF MATTHIAS H. KRAUS UNDER 37 C.F.R. § 1.132

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

NEEDLE & ROSENBERG, P.C.
Suite 1200
The Candler Building
127 Peachtree Street, N.E.
Atlanta, Georgia 30303-1811

March 31, 1995

Sir:

I, MATTHIAS H. KRAUS, declare as follows:

1. I am a co-inventor of the above referenced patent application.

2. It is my belief that increased expression of the MAC117 gene can be detected in body samples other than tissue or tumor cells. This belief is based upon the accompanying reference submitted herewith as Exhibit A: Leitzel, K. *et al.*, "Elevated soluble c-erbB-2 antigen levels in the serum and effusions of proportion of breast cancer patients." (*J. Clin.*

Oncol. **10** (9):1436-1443 (1992)). This reference discloses the detection of the protein product of the MAC117 (c-erbB-2) gene in serum and effusions from cancer patients. Specifically, this paper sets forth data from an enzyme linked immunosorbent assay (ELISA) assay developed to detect the extracellular domain of the c-erbB-2 oncogene product in serum and effusions from cancer patients. The assay data showed that sera from 12 of 53 patients with metastatic or locally advanced breast cancer, zero of 69 controls, one of 31 patients with ovarian cancer and two of 124 patients with other cancers had soluble c-erbB-2 levels greater than or equal to 5 U/ml. Also, two of five effusions from breast cancer patients had an elevated soluble c-erbB-2 antigen level, compared with zero of 17 effusions from patients with benign disease. These data establish evidence that the detection of increased expression of the MAC117 gene can be carried out by analyzing serum and effusion fluid as well as tissue or tumor cell samples.

3. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that any such willful false statement may jeopardize the validity of the application or any patent issued thereon.

M. Kraus, M.D.
MATTHIAS H. KRAUS

4/4/95
DATE

39826

DOCKET NUMBER 1414.025
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

KING et al.

Serial No. 07/110,791

Filed: October 21, 1987

For: HUMAN GENE RELATED TO BUT DISTINCT FROM EGF RECEPTOR GENE

Group Art Unit: 1807

Examiner: Marschel, A.

DECLARATION OF MATTHIAS H. KRAUS UNDER 37 C.F.R. § 1.132

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

NEEDLE & ROSENBERG, P.C.
Suite 1200
The Candler Building
127 Peachtree Street, N.E.
Atlanta, Georgia 30303-1811

April 3, 1995

Sir:

I, MATTHIAS H. KRAUS, declare as follows:

1. The above-identified application has been amended, based upon the recommendation of the Patent Office for the reason that the application contains improper incorporations by reference to the following publication:

Ullrich, A. *et al.* (May, 1984) *Nature* 309:418-425 (submitted as Exhibit B).

Specifically, the specification has been amended on page 8 to include the nucleotide sequence of the EGF receptor gene, as disclosed in the above reference.

2. The amendatory material consists of the same material incorporated by reference in the referencing application. Specifically, the amendments incorporate material contained in the reference cited in the specification at the following locations:

Page 2, lines 21-22

Page 3, lines 15-16

3. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that any such willful false statement may jeopardize the validity of the application or any patent issued thereon.

M. Kraus, M.D.
MATTHIAS H. KRAUS

4/4/95
DATE